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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,177	03/29/2004	Wei Gu	19240.431-US1	5834

56949 7590 01/22/2008  
WilmerHale/Columbia University  
399 PARK AVENUE  
NEW YORK, NY 10022

EXAMINER

FETTEROLF, BRANDON J

ART UNIT	PAPER NUMBER
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1642

MAIL DATE	DELIVERY MODE
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01/22/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/813,177	GU ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Brandon J. Fetterolf, PhD	1642	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 47,48,54,57 and 62-64 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 47, 48, 62-63 is/are allowed.
- 6) ☒ Claim(s) 54,57 and 64 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/30/2007 has been entered.

Claims 47-48, 54, 57 and 62-64 are currently pending and under consideration.

**All previous rejections are withdrawn in view of Applicants amendments.**

### **New Rejections:**

#### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54, 57 and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed

is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the nature of the invention, (2) the relative skill of those in the art, (3) the breadth of the claims, (4) the amount or direction or guidance presented, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the state of the prior art, and (8) the predictability or unpredictability of the art.

Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406) Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

**The nature of the invention**

The claims are drawn to a method of determining whether an agent is reactive with HAUSP or MDM2. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

**Level of skill in the art**

The level of skill in the art is deemed to be high, generally that of a master's or PhD.

**The breadth of the claims**

Applicants claim in claim 54 a method of determining whether an agent is reactive with MDM2, comprising the steps of: (a) contacting a candidate agent with Mdm2, in the presence of HAUSP; and (b) determining whether the candidate agent inhibits Mdm2-HAUSP protein complex formation, wherein determination of inhibition of Mdm2-HAUSP protein complex formation in (b) compared to Mdm2-HAUSP protein complex formation in the absence of the agent indicates that the agent is reactive with Mdm2. Alternatively, Applicants claim in claim 57 a method of determining whether an agent is reactive with HAUSP, comprising the steps of: (b) contacting a candidate agent with HAUSP, in the presence of MDM2; and (b) determining whether the candidate agent inhibits MDM2-HAUSP protein complex formation, wherein determination of inhibition of Mdm2-HAUSP protein complex formation in (b) compared to Mdm2-HAUSP protein complex formation in the absence of the agent indicates that the agent is reactive with HASUP. Thus, the claims broadly encompass determining whether an agent is reactive with 2 distinct proteins, HAUSP or MDM2, comprising performing the same steps.

**Guidance in the specification and Working Examples**

The specification teaches that the instant inventors have established a critical role for HAUSP in the control Mdm2 stability, wherein HAUSP is required for the stability of endogenous Mdm2, which is constitutively self-ubiquitinated and degraded in vivo (page 18, paragraph 0053). As such, the specification teaches that the instant invention encompasses a method of identifying a modulator of MDM2-HAUSP interaction by assessing the ability of a candidate modulator to affect (i.e., increase or decrease) Mdm2-HAUSP interaction, said method comprising the steps of: (a) obtaining or generating an in vitro system comprising Mdm2 and HAUSP; (b) contacting the in vitro system with a candidate modulator; and (c) determining if the candidate modulator modulates Mdm2-HAUSP interaction in the in vitro system (paragraph 00159). In addition, the specification further teaches that the instant invention encompasses methods of identifying agents which are

reactive with Mdm2 or HAUSP, comprising the steps of contacting a candidate agent with Mdm2 or HAUSP, in the presence of the other; and (b) assessing the ability of the candidate agent to inhibit HAUSP-Mdm2 interaction (paragraphs 00153 and 00157). Thus, while the specification appears to reasonably convey, in view of the method steps, a method of identifying agents which modulate Mdm2-HAUSP interaction, the specification does not appear to be commensurate in scope with the claimed invention which identifies inhibitors of two distinct proteins by performing the same steps. As such, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as written and identify an inhibitor of a specific protein.

Kinzler et al. (US 5,702,903, 1997, of record) teach a method for identifying compounds which interfere with the binding of human MDM2 to human p53 (column 33, Claim 1). Li et al. (Nature 2002; 416: 648-653, of record) teach that the deubiquitination of p53 by HAUSP is an important pathway for p53 stabilization. Together, Kinzler et al. and Li et al. are considered to be the closest prior art. However, the references alone or in combination do not appear to teach or suggest a method of identifying an agent that is reactive with HAUSP/MDM2, wherein the agent is in the presence of both MDM2 and HAUSP. As such, claims 47-48, 62-63 appear to be free of the prior art and are in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD  
Patent Examiner  
Art Unit 1642

A handwritten signature in black ink, reading "Brandon Fetterolf, PhD". The signature is stylized with a large, sweeping flourish at the end.

BF